FULBRIGHT & JAWORSKI L.L.P.
A REGISTERED LIMITED LIABILITY PARTNERSHIP
600 CONGRESS AVENUE, SUITE 2400
AUSTIN, TEXAS 78701-3271
WWW.FULBRIGHT.COM

STEVEN L. HIGHLANDER
PARTNER
SHIGHLANDER@FULBRIGHT.COM

DIRECT DIAL: (512) 536-3184
TELEPHONE: (512) 474-5201
FACSIMILE: (512) 536-4598

March 2, 2004

CERTIFICATE OF MAILING
37 C.F.R 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: MS DD, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below:

March 2, 2004 — Steven L. Highlander
Date

MS DD
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

RE: *U.S. Patent Application No. 10/743,697 entitled "BISPECIFIC ANTIBODIES" – Peter Kufer et al.*
Our reference: DEBE:028US
Client reference: MIC-020US

Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, Form PTO-1449, and references A1-A2, B1-B2 and C1-C23.

No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to the enclosed materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/DEBE:028US.

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

Steven L. Highlander
Reg. No. 37,642

SLH/kmv
Encl.: as noted

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Peter Kufer *et al.*	Group Art Unit: Unknown
Serial No.: 10/743,697	Examiner: Unknown
Filed: December 22, 2003	Atty. Dkt. No.: DEBE:028US
For: BISPECIFIC ANTIBODIES	

CERTIFICATE OF MAILING
37 C.F.R 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to:, MS DD, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below:

March 2, 2004
Date

Steven L. Highlander

INFORMATION DISCLOSURE STATEMENT

MS DD
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner.

In accordance with 37 C.F.R §§ 1.97(g), (h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R § 1.97(b). No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/DEBE:028US.

Applicants respectfully request that the listed documents be made of record in the present case.

Respectfully submitted,

Steven L. Highlander
Reg. No. 37,642
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 474-5201

Date: March 2, 2004

Form PTO-1449 (modified)	Atty. Docket No. DEBE:028US	Serial No. 10/743,697
List of Patents and Publications for Applicant's INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	Applicant Peter Kufer *et al.*	
	Filing Date: December 22, 2003	Group: Unknown

U.S. Patent Documents	Foreign Patent Documents	Other Art
See Page 1	*See Page 1*	*See Page 1*

U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.
	A1	5,258,498	11/02/93	Huston and Oppermann	530	350	5/19/88
	A2	5,525,491	6/11/96	Huston *et al.*	435	69.7	6/09/94

Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No
	B1	EP 573 551	5/21/03	Europe			
	B2	EP 623 679	11/09/94	Europe			

Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Baynex, "Recombinant protein expression in Escherichia coli," *Curr. Opin. Biotech.*, 10:411-421, 1999.
	C2	Bohlen *et al.*, "Cytolysis of Leukemic B-cells by T-cells activated via two bispecific antibodies," *Cancer Res.*, 53:4310-4314, 1993.
	C3	Brühl, "Deplection of CCR5-expressing cells with bispecific antibodies and chemokine toxins: a new strategy in the treatment of chronic inflammatory diseases and HIV," *J. Immunol.*, 166:2420-2406, 2001.
	C4	Cortez-Retamozo *et al.*, "Efficient tumor targeting by single-domain antibody fragments of camels," *Int. J. Cancer*, 98:456-462, 2002.
	C5	Davies and Reichmann, "Antibody VH domains as small recognition units," *Biotechnology*, 13:475-479, 1995.
	C6	Davies and Riechmann, "Single antibody domains as small recognition units: design and in vitro antigen selection of camelized, human VH domains with improved protein stability," *Protein Engineering*, 9(6):531-537, 1996.

25373241.1

EXAMINER:	DATE CONSIDERED:

EXAMINER: INITIAL IF REFERENCE CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED. INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

Form PTO-1449 (modified)	Atty. Docket No. DEBE:028US	Serial No. 10/743,697
List of Patents and Publications for Applicant's INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	Applicant Peter Kufer *et al.*	
	Filing Date: December 22, 2003	Group: Unknown

U.S. Patent Documents	Foreign Patent Documents	Other Art
See Page 1	*See Page 1*	*See Page 1*

Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C7	De Jonge *et al.*, "In vivo retargeting of T cell effector function by recombinant bispecific single chain Fv (anti-CD3 x anti-idiotype) induces long-term survival in the murine BCL1 lymphoma model," *J. Immunol.*, 161:1454-1461, 1998.
	C8	Desmyter *et al.*, "Antigen specificity and high affinity binding provided by one single loop of a camel singe-domain antibody," *J. Biol. Chem.*, 276(28):26285-26290, 2001.
	C9	Destmyter *et al.*, "Three camelid VHH domains in complex with porcine pancreatic α-amylase," *J. Biol. Chem.*, 277(26):23645-23650, 2002.
	C10	Dumoulin *et al.* "Single-domain antibody fragments with high conformational stability," *Protein Science*, 11:500-515, 2002.
	C11	Conrath *et al.*, "Camel single-domain antibodies as modular building units in bispecific and bivalent antibody constructs," *J. Biol. Chem.*, 276(10):7346-7350, 2001.
	C12	Ewert *et al.*, "Biophysical properties of camelid VHH domains compared to those of human VH3 domains," *Biochemistry*, 41:3628-3636, 2002.
	C13	Harmsen *et al.*, "Llama heavy-chain V regions consist of at least four distinct subfamilies revealing novel sequence features," *Molecular Immunology*, 37:579-590, 2000.
	C14	Jobling *et al.*, "Immunomodulation of enzyme function in plants by single-domain antibody fragments," *Nature Biotech.*, 21:77-80, 2003.
	C15	Kufer *et al.*, "Construction and biological activity of a recombinant bispecific single-chain antibody designed for therapy of minimal residual colorectal cancer," *Cancer Immunol. Immunother.*, 45:193-197, 1997.
	C16	Löffer *et al.*, "A recombinant bispecific single-chain antibody, CD19 x CD3, induces rapid and high lymphoma-directed cytotoxicity by unstimulated T lymphocytes," *Blood*, 95(6):2098-2103, 2000.
	C17	Mack *et al.*, "Biologic properties of a bispecific single-chain antibody directed against 17-1A (EpCAM) and CD3," *J. Immunol.*, 158:3965-3970, 1997.
	C18	Mack *et al.*, "A small bispecific antibody construct expressed as a functional single-chain molecule with high tumor cell cytotoxicity," *Proc. Natl. Acad. Sci., USA*, 92:7021-7025, 1995.

25373241.1

EXAMINER:	DATE CONSIDERED:

EXAMINER: INITIAL IF REFERENCE CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED. INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

Form PTO-1449 (modified)	Atty. Docket No. DEBE:028US	Serial No. 10/743,697
List of Patents and Publications for Applicant's INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	Applicant Peter Kufer *et al.*	
	Filing Date: December 22, 2003	Group: Unknown

U.S. Patent Documents	Foreign Patent Documents	Other Art
See Page 1	*See Page 1*	*See Page 1*

Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C19	Muruganandam *et al.*, "Selection of phage-displayed llama single-domain antibodies that transmigrate across human blood-brain barrier endothelium," *FASEB Journal*, 16:240-242, 2002.
	C20	Muyldermans *et al.*, "Recognition of antigens by single-domain antibody fragments: the superfluous luxury of paired domains," *Trends in Biochemical Sciences*, 26(4):230-235, 2001.
	C21	Riechmann, "Rearrangement of the former VL interface in the solution structure of a camelised, single antibody VH domain," *J. Mol. Biol.*, 259:957-969, 1996.
	C22	Spinelli *et al.*, "Camelid heavy-chain variable domains provide efficient combining sites to haptens," *Biochemistry*, 39:1217-1222, 2000.
	C23	Tanha *et al.*, "Optimal design features of camelized human single-domain antibody libraries," *J. Biol. Chem.*, 276(27):24774-24780, 2001.

25373241.1

EXAMINER:	DATE CONSIDERED:

EXAMINER: INITIAL IF REFERENCE CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED. INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.